FIGURE 1

Sheet 1 of 3

```
                                  ____________ I ____________                                    __ II __
human EP2K      122 SEWLDEEVLIFKNAQLAPICGAIYREFFKNFLHAQ------------------------------------QVKGAIDVVAKRYIEDICL
C. e. EP2K      108 KQWTEDCVSLHTDIPASGAIREIYPLKKDSKHQTSQ------------------------------------DIK--SSIDVVAKRYIQQVD
MHCK A          570 NFWIELNFLNVEFPPASGALREAYNTVGLDVVTCENVPLSTTTKLPPPIENCIPPCSFDSREAMTQLKSNTKFVLELVNEEAI
MHCK B          130 AQWTSTATLVNVEFPPASGAFRFAYHTLDLSKSGA------------------------------------SDPYVTKIQKK---
FC-AN09           1       DVTVSIEETTPANGGCRTAMKLKDMGQP------------------------------------DQGLVTKPSTRKK-
consensus           **W******o*o****F**G**R**o**************************************************oV*K*******

                                  ____________ III ____________                                  ____ IV ____
human EP2K      178 ----RDVYPEDVPLQNEAKLWGEEYNRHKPPKQVDIMQHCIIELKDR----PGKPLP-HLEHYIEGKYIKVNSMSGFVPDDNI
C. e. EP2K      162 ----RPVLPSDVPLQNDAKLWAEEYMRYNPPKKIDIVQHCVIEMIDV----KGSPLY-HLEHPIEGKYIKVNSMSGFVSNAA-
MHCK A          653 QQASRELYPEDVPMQMVCPSWGNKPMQKKPPKKIEPLHSWVVELIDRSPSSNGQPILCSIEPLLVQEPYSDVNSMTGAVLTN--
MHCK B          177 -PTPRPSYPEDVPMQHIAKKWACKYMSFKPPKKIEPLQSCVLEPVDRTSSD----LICGAEPYVEQVYPKTNMNSGFVSNDE-
FC-AN09          42 --TTRCSYPTDVPMQTFCARWAEYPMEAKPPKPITPLPSYVYELIDHPPPY---PV-CGGEPPIEGEYYEKNMNSGTVSSDA-
consensus           ****R**oP*DV*oQ*****W***oN***PPK*o*oo***ooEo*D*********o****E*oo*G*o*K*N*M*G*V*****

                                                  ____________ V ____________ ____________ VI ____________
human EP2K      252 RLTPQAPSHPTYEPSRHPQLIVVDIQGVCDLYTDPQIHTSTGTCPGCGMLQTRQMALPPYSMACNRICESMGLAPPDLSPPIPP
C. e. EP2K      235 RLTPQAPSHPTYEPSRHPQMKVVDIQGVCDLYTDPQIHTPVGTCYGCGMLQTRQMALPPNSMPCNDICETMCLSMPELSPPEIP
MHCK A          734 RSTPQAPSHPTYRLSNKPQMIVVDIQGVCDLYTDPQIHTPCGKCPGLGNLQKAQINEPITTMKCNAVCALLCL-DVKLG-----
MHCK B          254 RVTPQSPSHPTYEHSNHPQLLIIDIQGVCDHYTDPQIHTYCGVCPGIGNLQCKQPSYPLDTMKCNAICQYLNLQSIN-------
FC-AN09         118 RVTPQSPSHPSYELSNHELLIVDIQGVCNDFYTDPQIHTKSGECPGEGNLGETGPHKPLQTEKCNTVCSFLKLKPIN-------
consensus           R*TPQ*PSHP*oE*S***ooooDIQGV*DoYTDPQIHT**G**oG*GNLG**Go**Po**E*CN*oC**o*L**o********

                                                  ___ VII ___
human EP2K      335 AVNQITKLLQSAK---LPSTEEKCSS
C. e. EP2K      318 ATEVAMEVAAKQKISCVPPTVEAPP
MHCK A          811 ----GVLSGINFKQ---LQQSTVCMDDI
MHCK B          330 --------PKSEKSSC---STVPPPDL
FC-AN09         194 ---------QSVKA---LLPSTLPVVQL
consensus           ***********K*******T******
```

a

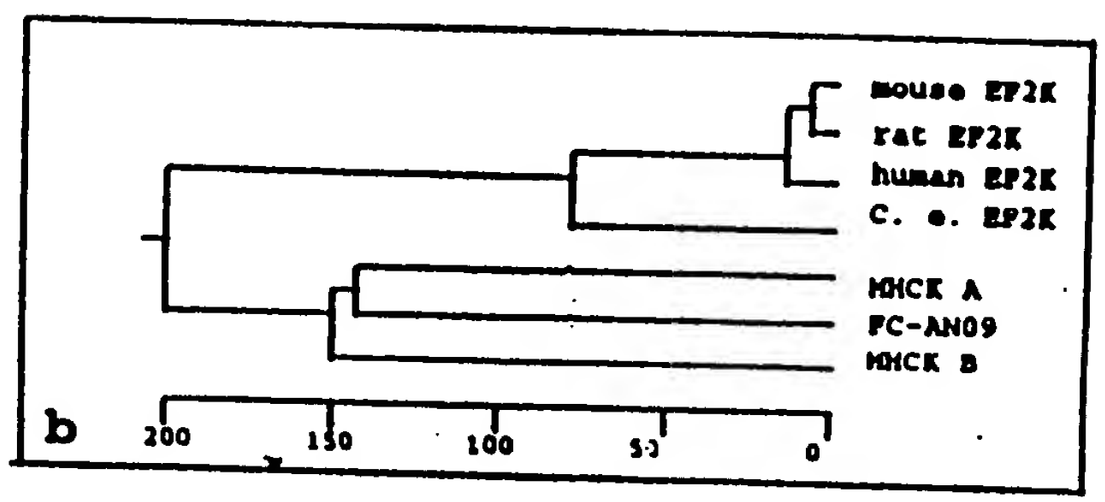

FIGURE 2

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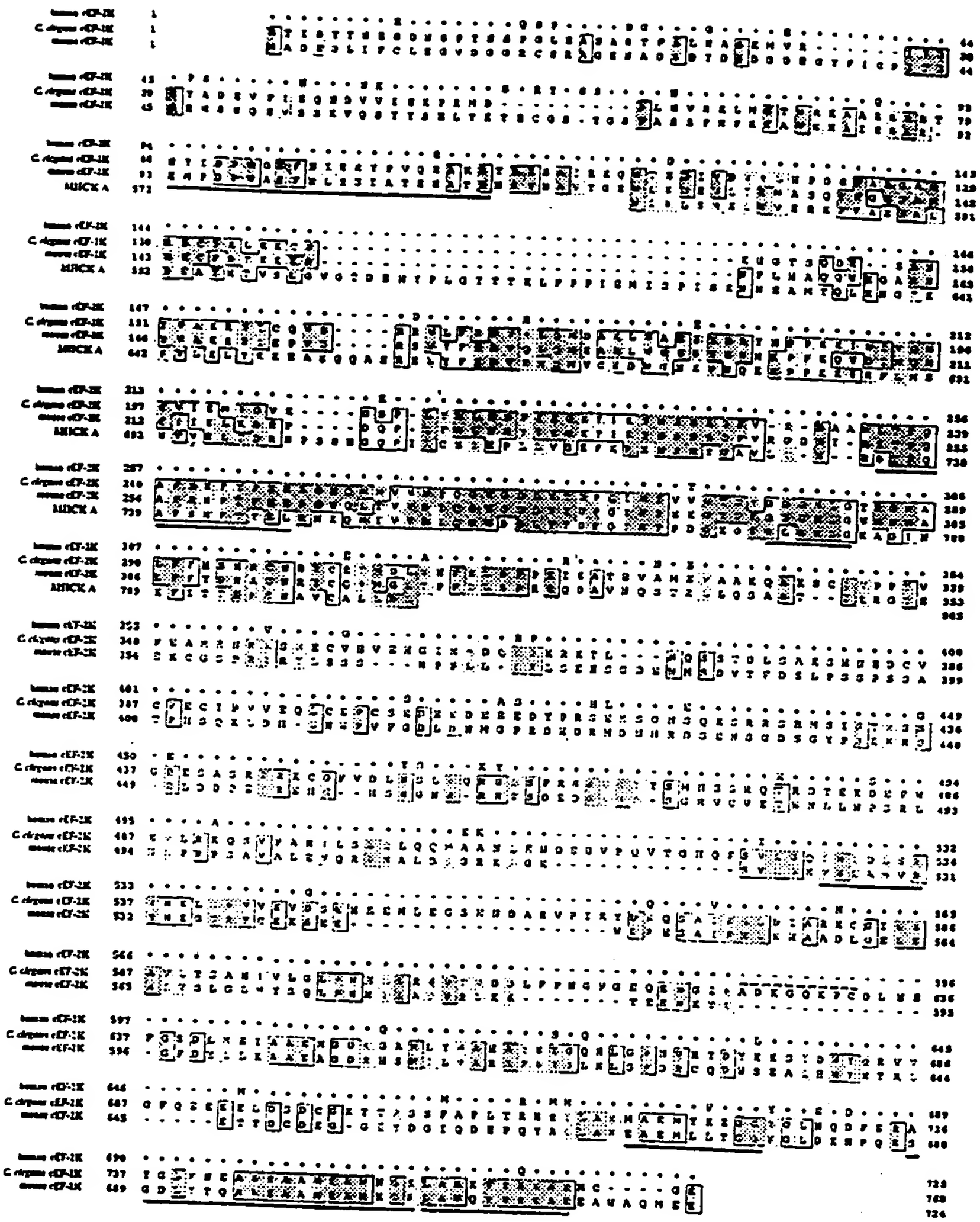

FIGURE 3

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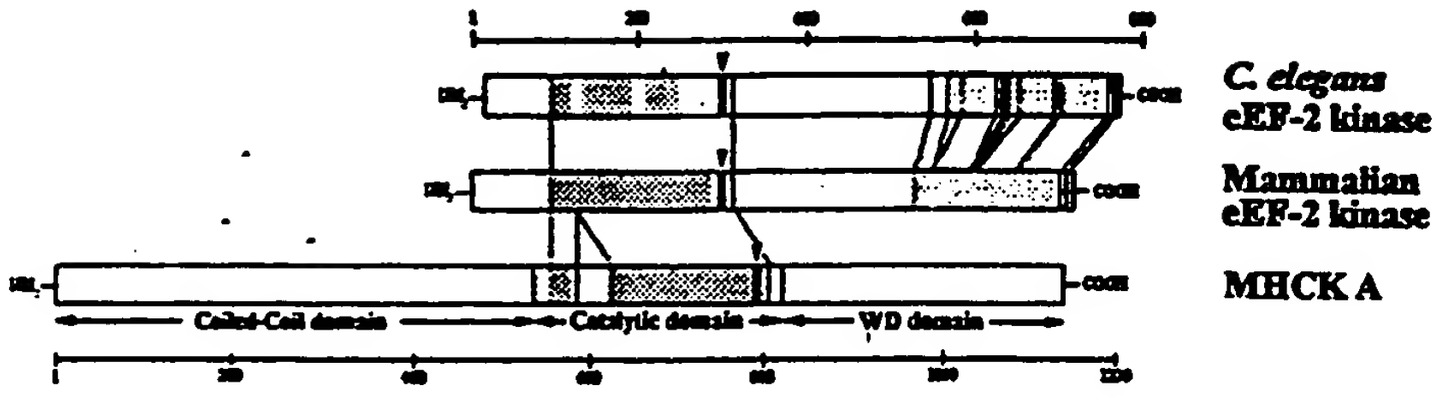

***C. elegans* eEF-2 kinase**

Mammalian eEF-2 kinase

MHCK A

FIGURE 4

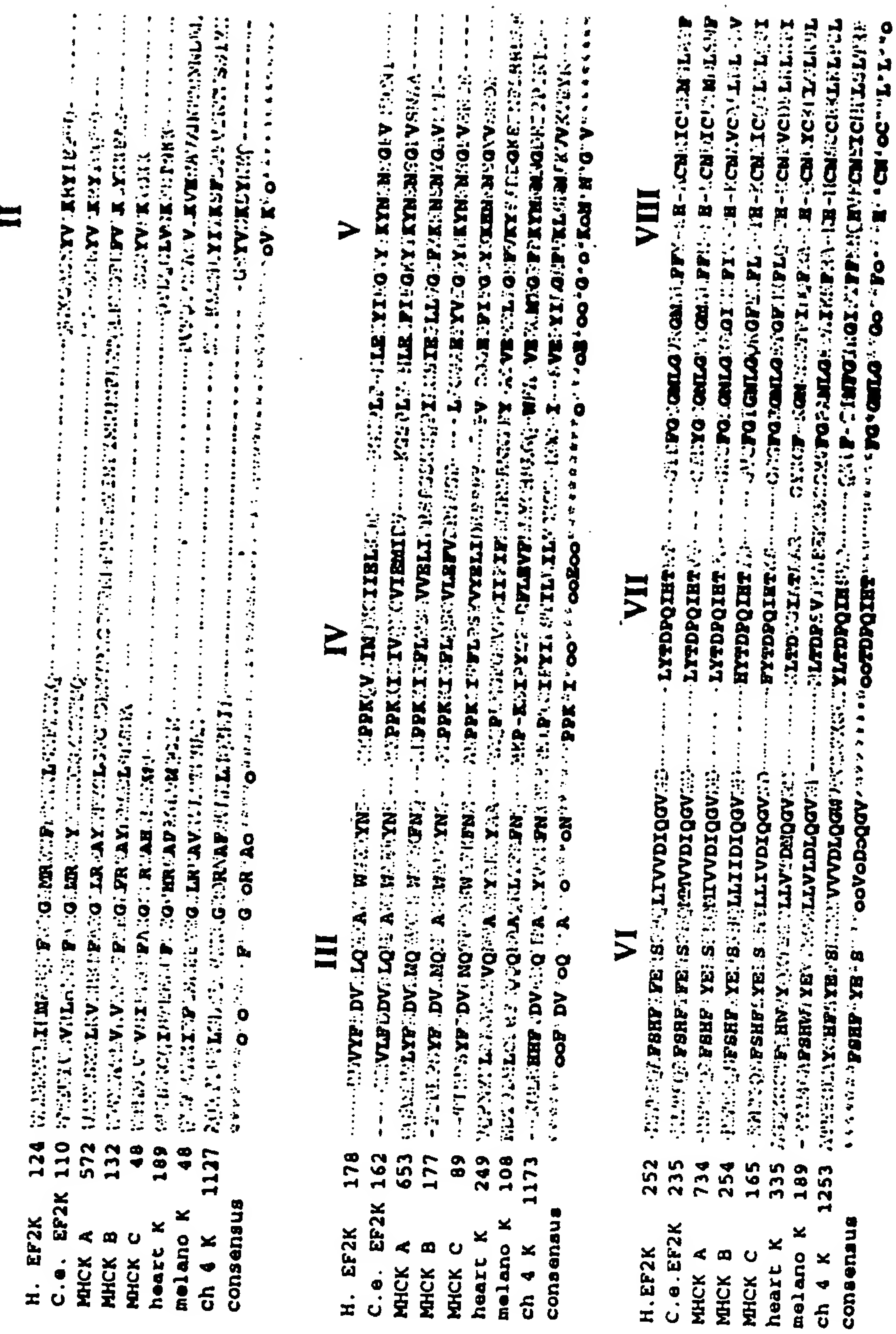
I
II
III
IV
V
VI
VII
VIII
H. EF2K
C.e. EF2K
MHCK A
MHCK B
MHCK C
heart K
melano K
ch 4 K
consensus

FIGURE 5A

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```
   1 cgggcgcggg cgcgtccctc tggccagtca cccggcggag ctggtcgcac aattatgaaa
  61 gactcgactt ctgctgctag cgctggagct gagttagttc tgagaaggtt tcccggggct
 121 gtccttgttc ggtggcccgt gccaccgcct ccggagacgc tttccgatag gtggctgcag
 181 gccgcggagg tggaggagga gccgctgccc ttccggagtc cgccccgtga ggagaatgtc
 241 ccagaaatcc tggatagaga gcactttgac caagagggag tgtgtatata ttataccaag
 301 ctccaaagac cctcacagat gtcttccagg atgtcagatt tgtcagcaac ttgtcagatg
 361 tttctgtggt cgtttggtca agcaacatgc atgctttact gcaagtcttg ccatgaaata
 421 ctcagatgtg agattgggtg aacactttaa ccaggcaata gaagaatggt ctgtggaaaa
 481 gcacacggag cagagcccaa cagatgctta tggagtcatc aattttcaag ggggttctca
 541 ttcctacaga gctaagtatg tgagactatc atatgatacc aaacctgaaa tcattctgca
 601 acttctgctt aaagaatggc aaatggagtt acccaaactt gttatttctg tacatggagg
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1681 aggtccaacc aatccaatgt tgttccatct cattcgggat gtcaagcagg gtaatctccc
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3181 aaatcaacag gcaggacctt atgtaatgat gattggaaaa atggtggcca atatgttcta
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```

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6361 aacccagggc ctcatgaaga ccattttcta agagacattt tatttaagaa tcaactatag
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6481 ttttttaaca tttatcaatg ttaagtaaaa gaaagccatg ataaataaga attaactcac
6541 tgttcaatgg gtgtttcctg tgaggaaggt tacagttgta acagcctgca gttgcataca
```

FIGURE 5C

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C

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CIP

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6961 gagataagct gttaaatagt gtttaatgtt gatgtggaga gaaaggtgta ttacttaaaa
7021 atactatacc atatacgttt tgtatatcat taaatcttta aaagaaatta aatttattct
7081 tgtttacaaa
```

FIGURE 6A

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CIP

MSQKSWIESTLTKRECVYIIPSSKDPHRCLPGCQICQQLVRCFCGRLVKQHACFTASLAM

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LQLLLKEWQMELPKLVISVHGGMQKFELHPRIKQLLGKGLIKAAVTTGAWILTGGVNTGV

AKHVGDALKEHASRSSRKICTIGIAPWGVIENRNDLVGRDVVAPYQTLLNPLSKLNVLNN

LHSHFILVDDGTVGKYGAEVRLRRELEKTINQQRIHARIGQGVPVVALIFEGGPNVILTV

LEYLQESPPVPVVVCEGTGRAADLLAYIHKQTEEGGNLPDAAEPDIISTIKKTFNFGQSE

AVHLFQTMMECMKKKELITVFHIGSEDHQDIDVAILTALLKGTNASAFDQLILTLAWDRV

DIAKNHVFVYGQQWLVGSLEQAMLDALVMDRVSFVKLLIENGVSMHKFLTIPRLEELYNT

KQGPTNPMLFHLIRDVKQGNLPPGYKITLIDIGLVIEYLMGGTYRCTYTRKRFRLIYNSL

GGNNRRSGRNTSSSTPQLRKSHETFGNRADKKEKMRHNHFIKTAQPYRPKMDASMEEGKK

KRTKDEIVDIDDPETKRFPYPLNELLIWACLMKRQVMARFLWQHGEESMAKALVACKIYR

SMAYEAKQSDLVDDTSEELKQYSNDFGQLAVELLEQSFRQDETMAMKLLTYELKNWSNST

CLKLAVSSRLRPFVAHTCTQMLLSDMWMGRLNMRKNSWYKVILSILVPPAILMLEYKTKA

EMSHIPQSQDAHQMTMEDSENNFHNITEEIPMEVFKEVKILDSSDGKNEMEIHIKSKKLP

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VREVFMSEAGKISQKIKVWFSDYFNVSDTIAIISFFVGFGLRFGAKWNYINAYDNHVFVA

GRLIYCLNIIFWYVRLLDFLAVNQQAGPYVMMIGKMVANMFYIVVIMALVLLSFGVPRKA

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LFCCVCKRRKKDKTSDGPKLFLTEEDQKKLHDFEEQCVEMYFDEKDDKFNSGSEERIRVT

FERVEQMSIQIKEVGDRVNYIKRSLQSLDSQIGHLQDLSALTVDTLKTLTAQKASEASKV

HNEITRELSISKHLAQNLIDDVPVRPLWKKPSAVNTLSSSLPQGDRESNNPFLCNIFMKD

EKDPQYNLFGQDLPVIPQRKEFNIPEAGSSCGALFPSAVSPPELRQRRHGVEMLKIFNKN

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FIGURE 6B

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CIP

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LRRAVKVLCTWSEHDILKSGHLYIIKSFLPEVINTWSSIYKEDTVLHLCLREIQQQRAAQ

KLTFAFNQMKPKSIPYSPRFLEVFLLYCHSAGQWFAVEECMTGEFRKYNNNNGDEIIPTN

TLEEIMLAFSHWTYEYTRGELLVLDLQGVGENLTDPSVIKAEEKRSCDMVFGPANLGEDA

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Figure 7B

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Figure 8A

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Figure 8B

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1201  ttaaatctgg caatggcttg ggacagggtg gacattgcca agaaacatat cctaatttat
1261  gaacaacact ggaagcctga tgccctggaa caagcaatgt cagatgcttt agtgatggat
1321  cgggtggatt ttgtgaagct cttaatagaa tatggagtga acctccatcg ctttcttacc
1381  atccctcgac tggaagagct ctacaataca aaacaaggac ctactaatac actcttgcat
1441  catctcgtcc aagatgtgaa acagcatacc cttctttcag gctaccgaat aaccttgatt
1501  gacattggat tagtagtaga atacctcatt ggtagagcat atcgcagcaa ctacactaga
1561  aaacatttca gagccctcta caacaacctc tacagaaaat acaagcacca gagacactcc
1621  tcaggaaata gaaatgagtc tgcagaaagt acgctgcact cccagttcat tagaactgca
1681  cagccataca aattcaagga aaagtctata gtccttcata aatcaaggaa gaagtcaaaa
1741  gaacaaaatg tatcagatga ccctgagtct actggctttc tttacccttа caatgacctg
1801  ctggtttggg ctgtgctgat gaaaaggcag aagatggcta tgttcttctg gcagcatgga
1861  gaggaggcca cggttaaagc cgtgattgcg tgtatcctct accgggcaat ggcccatgaa
1921  gctaaggaga gtcacatggt ggatgatgcc tcagaagagt tgaagaatta ctcaaaacag
1981  tttggccagc tggctctgga cttgttggag aaggcattca agcagaatga gcgcatggcc
2041  atgacgctgt tgacgtatga actcaggaac tggagcaatt cgacctgcct taaactggcc
2101  gtgtcgggag gattacgacc ctttgtttca catacttgta cccagatgct actgacagac
2161  atgtggatgg ggaggctgaa aatgaggaaa aactcttggt taaagattat tataagcatt
2221  attttaccac ccaccatttt gacactggaa tttaaaagca aagctgagat gtcacatgtt
2281  ccccagtccc aggacttcca atttatgtgg tattacagtg accagaacgc cagcagttcc
2341  aaagaaagtg cttctgtgaa agagtatgat ttggaaaggg gccatgatga gaaactggat
2401  gaaaatcagc attttggttt ggaaagtggg caccaacacc ttccgtggac caggaaagtc
2461  tatgagttct acagtgctcc aattgtcaag ttttggtttt atacgatggc gtatttggca
2521  ttcctcatgc tgttcactta caccgtgttg gtggagatgc agccccagcc cagcgtgcag
2581  gagtggcttg ttagcattta catcttcacc aatgctattg aggtggtcag ggaggtgagt
2641  atttcagaac ctgggaagtt tacccaaaag gtgaaggtat ggattagtga gtactggaac
2701  ttaacagaaa ctgtggccat tggcctgttt tcagctggct tcgtccttcg atggggtgac
2761  cctccttttc acacagcggg aagactgatc tactgcatag acatcatatt ctggttctca
2821  cggctcctgg acttctttgc tgtgaatcaa catgcaggtc catatgtgac catgattgca
2881  aaaatgacag caaacatgtt ctatattgtg atcatcatgg ccatagtcct gctgagcttt
2941  ggagtggcac gcaaggccat cctttcgcca aaagagccac catcttggag tctagctcga
3001  gatattgtat ttgagccata ctggatgata tacggagaag tctatgctgg agaaatagat
3061  gtttgttcaa gccagccatc ctgccctcct ggttcttttc ttactccatt cttgcaagct
3121  gtctacctct tcgtgcaata tatcatcatg gtgaacctgt tgattgcttt cttcaacaac
3181  gtttacttag atatggaatc catttcaaat aacctgtgga aatacaaccg ctatcgctac
3241  atcatgacct accacgagaa gccctggctg ccccccacctc tcatcctgct gagccacgtg
3301  ggccttctcc tccgccgcct gtgctgtcat cgagctcctc acgaccaaga agagggtgac
3361  gttggattaa aactctacct cagtaaggag gatctgaaaa aacttcatga ttttgaggag
3421  cagtgcgtgg aaaaatactt ccatgagaag atggaagatg tgaattgtag ttgtgaggaa
3481  cgaatccgag tgacatcaga aagggttaca gagatgtact tccagctgaa agaaatgaat
3541  gaaaaggtgt cttttataaa ggactcctta ctgtctttgg acagccaggt gggacacctg
3601  caggatctct ctgccctgac tgtggatacc ctgaaagtcc tttctgctgt tgacactttg
3661  caagaggatg aggctctcct ggccaagaga aagcattcta cttgcaaaaa acttccccac
3721  agctggagca atgtcatctg tgcagaggtt ctaggcagca tggagatcgc tggagagaag
3781  aaataccagt attatagcat gccctcttct ttgctgagga gcctggctgg aggccggcat
3841  cccccaagag tgcagagggg ggcacttctt gagattacaa acagtaaaag agaggctaca
3901  aatgtaagaa atgaccagga aaggcaagaa acacaaagta gtatagtggt ttctggggtg
3961  tctcctaaca ggcaagcaca ctcaaagtat ggccagtttc ttctggtccc ctctaatcta
```

Figure 9A

4021 aagcgagttc cttttcagc agaaactgtc ttgcctctgt ccagaccctc tgtgccagat
4081 gtgctggcaa ctgaacagga catccagact gaggttcttg ttcatctgac tgggcagacc
4141 ccagttgtct ctgactgggc atcagtggat gaacccaagg aaaagcacga gcctattgct
4201 cacttactgg atggacaaga caaggcagag caagtgctac ccactttgag ttgcacacct
4261 gaacccatga caatgagctc ccctctttcc caagccaaga tcatgcaaac tggaggtgga
4321 tatgtaaact gggcattttc agaaggtgat gaaactggtg tgtttagcat caagaaaaag
4381 tggcaaacct gcttgccctc cacttgtgac agtgattcct ctcggagtga acagcaccag
4441 aagcaggccc aggacagctc cctatctgat aactcaacaa gatcggccca gagtagtgaa
4501 tgctcagagg tgggaccatg gcttcagcca aacacatcct tttggatcaa tcctctccgc
4561 agatacaggc ccttcgctag gagtcatagt tttagattcc ataaggagga gaaattgatg
4621 aagatctgta agattaaaaa tctttcaggc tcttcagaaa tagggcaggg agcatgggtc
4681 aaagcgaaaa tgctaaccaa agacaggaga ctgtcaaaga aaaagaagaa tactcaagga
4741 ctccaggtgc caatcataac agtcaatgcc tgctctcaga gtgaccagtt gaatccagag
4801 ccaggagaaa acagcatctc tgaagaggag tacagcaaga actggttcac agtgtccaaa
4861 tttagtcaca caggtgtaga accttacata catcagaaaa tgaaaactaa agaaattgga
4921 caatgtgcta tacaaatcag tgattaccta aagcagtctc aagaggatct cagcaaaaac
4981 tctttgtgga attccaggag caccaacctc aataggaact ccctgctgaa aagttcaatt
5041 ggagttgaca agatctcagc ctccttaaaa agccctcaag agcctcacca tcattattca
5101 gccattgaaa ggaataattt aatgaggctt tctcagacca taccatttac accagtccaa
5161 ctgtttgcag gagaagaaat aactgtctac aggttggagg agagttcccc tttaaacctt
5221 gataaaagca tgtcctcttg gtctcagcgt gggagagcgg caatgatcca ggtattgtcc
5281 cgagaggaga tggatggggg cctccgtaaa gctatgagag tcgtcagcac ttggtctgag
5341 gatgacattc tcaagccggg acaagtttte attgtcaagt cctttcttcc tgaggttgtg
5401 cggacatggc ataaaatctt ccaggagagc actgtgcttc atctttgcct cagggaaatt
5461 caacaacaaa gagctgctca aaaattgatc tataccttca accaagtgaa accacaaacc
5521 ataccctaca caccaaggtt cctggaagtt ttcttaatct actgccattc agccaaccag
5581 tggttgacca ttgagaagta tatgacaggg gagttccgga agtataacaa caacaatggt
5641 gatgaaatca cccccaccaa caccctggag gagctgatgt tggctttctc tcactggacc
5701 tatgagtaca ctcggggaga gctgctggtt ttagatttgc aaggtgttgg agaaaatttg
5761 acagatccat ctgttataaa acctgaagtc aaacaatcaa gaggaatggt gtttggaccg
5821 gccaatttgg gggaagatgc aattagaaac ttcattgcaa aacatcattg taactcctgc
5881 tgccggaagc tcaaactccc ggatttaaaa agaaatgact attccccctga aaggataaat
5941 tccacctttg gacttgagat aaaaatagaa tcagctgagg agcctccagc aagggagacg
6001 ggtagaaatt ccccagaaga tgatatgcaa ctataaaaag ggaggagcaa gaagatccca
6061 gtgcttgccc tgcctgccag gaactctgtg ataacataga ttgatcaacg tgatgttgat
6121 tacatcagcg tctccttggg acacgccttc tgagcctcac atctccttct gttcaaaggc
6181 ctcattggta tatgatcaat gggttctcct agacactgac ctctgtccag ggcactttgc
6241 agctccatcc tcaagttcca cacgaagatg cttggatgag tcagctggga atattgttct
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6361 aggatggggt tgggggggat acatttattt tattttctca ctatgtatgc agactggacc
6421 ccctactact atttgtcacc tcacccacag attgtattta tgtctatata tatgttcata
6481 aaaagttatg tgatttcctc ctctgtcttt tccacaacat aggactttga atagcaatga
6541 taggaaaaac aatggaacaa gggtgggttt gcacagattg gagcacattc ctgcacaaac
6601 taccaagtat actggtgaaa tctcgatggg tttcagatat tgtcagtgaa tcatatgatg
6661 cctggatatt tcaggtttct gtaaaagaaa gggaaaccta aaacaaatac ccttccatat
6721 ataatatata tggaatatgt atattatata tatttttata tatataatat atatggaata
6781 tatatattat atatataaaa tacatatgga atatatatat tttatatata tatatatatt
6841 tttatttttg agatggagtt tcactctttt tacccaggct ggagtgcaat gatgcgatct
6901 cactgcaacc tctgcctccc gggcttgagc gattcttgtg tctcagtctt ccgggtagct
6961 gggactacag gtgtgcacca ctatgcctgg ctaattttgt atttttagta gagatggggt
7021 ttcaccatgt tggccaggct ggtctcaaac tcctgacctc agatgatcca cctgccttgg
7081 cttcccaaag tgctgggatt acaggcgtga gccactgcgc ctggcctttt ttttttttt
7141 tttaaacgag aacaagaata tgaagaactg gaaatcatta agaaagggtt tcccttcctt
7201 aaagctcagg ggtactatta gttaggagtt gactaactca acctgtaaaa caccactcct
7261 ccttccaaag ttgtatatat aatattgcag gttaaattac tttatgtcag gtcctatgaa
7321 gaaagatacg gtttcagact gaaaacatgt ttcacaggtg tttgcttcct tccagagcag
7381 agttccctat tccccctggca taaagaatgt atatatattt tgaaatatgg ctgagaacat
7441 gtcattggtt tgtgaggcct aaggtgaagc actcctggca gccacactgt gtagtgtatt
7501 tgagggatca gtcatccctc ttgtatgctg ggcctggttg ccctacctcg aacaagcacc
7561 agcttttcac acaaggagag atgtggggct gggagtcctc tccccatcct attgcatctc
7621 ctttcttatt ataagctgtt ccagttcaca ggcagcaaac ctcctgggtt tgaaaaattc
7681 caacttattt ttatctttaa tcctgacatt agctgacttg ctagtgagct tgctttaaaa
7741 atctacactc ttgcattctt aggcatacag gggaaatgtt gaaaaggaag gtggaaaacc
7801 aagaatttag tttgccaatg attgcctctg attcttgtaa gtttgagttc cacaagggct
7861 aatttattcc ccttttactt gggttttggg gtggtggaaa gcgggaaatt tgggtgattt
7921 gttgattggc aatgaggata aaatgttaat acttttttgg ggacttaaca actttatcct
7981 attctacaag tcagtaaagg aacaattggt actcacctca gtgctgcact caactatgga

Figure 9A

```
8041    aagaggcaga gtttgcttgc ccaattgcca aactaaagac atcagttcat tggtcaaata
8101    ttgttacct ggaatggaac ttgaaagcaa atacatttgg atttcaaatt tcaaaaaa
```

Figure 9A

Human kidney kinase

MSQKSWIKGVFDKRECSTIIPSSKNPHRCTPVCQVCQNLIRCYCGRLIGDHAGIDYSWTIS
AAKGKESEQWSVEKHTTKSPTDTFGTINFQDGEHTHHAKYIRTSYDTKLDHLLHLMLKE
WKMELPKLVISVHGGIQNFTMPSKFKEIFSQGLVKAAETTGAWIITEGINTVSKHVGDAL
KSHSSHSLRKIWTVGIPPWGVIENQRDLIGKDVVCLYQTLDNPLSKLTTLNSMHSHFILS
DDGTVGKYGNEMKLRRNLEKYLSLQKIHCRSRQGVPVVGLVVEGGPNVILSVWETVKD
KDPVVVCEGTGRAADLLAFTHKHLADEGMLRPQVKEEIICMIQNTFNFSLKQSKHLFQIL
MECMVHRDCITIFDADSEEQQDLDLAILTALLKGTNLSASEQLNLAMAWDRVDIAKKHI
LIYEQHWKPDALEQAMSDALVMDRVDFVKLLIEYGVNLHRFLTIPRLEELYNTKQGPTN
TLLHHLVQDVKQHTLLSGYRITLIDIGLVVEYLIGRAYRSNYTRKHFRALYNNLYRKYK
HQRHSSGNRNESAESTLHSQFIRTAQPYKFKEKSIVLHKSRKKSKEQNVSDDPESTGFLY
PYNDLLVWAVLMKRQKMAMFFWQHGEEATVKAVIACILYRAMAHEAKESHMVDDAS
EELKNYSKQFGQLALDLLEKAFKQNERMAMTLLTYELRNWSNSTCLKLAVSGGLRPFV
SHTCTQMLLTDMWMGRLKMRKNSWLKIIISIILPPTILTLEFKSKAEMSHVPQSQDFQFM
WYYSDQNASSSKESASVKEYDLERGHDEKLDENQHFGLESGHQHLPWTRKVYEFYSAP
IVKFWFYTMAYLAFLMLFTYTVLVEMQPQPSVQEWLVSIYIFTNAIEVVREVSISEPGKF
TQKVKVWISEYWNLTETVAIGLFSAGFVLRWGDPPFHTAGRLIYCIDIIFWFSRLLDFFA
VNQHAGPYVTMIAKMTANMFYIVIIMAIVLLSFGVARKAILSPKEPPSWSLARDIVFEPY
WMIYGEVYAGEIDVCSSQPSCPPGSFLTPFLQAVYLFVQYIIMVNLLIAFFNNVYLDMESI
SNNLWKYNRYRYIMTYHEKPWLPPPLILLSHVGLLLRRLCCHRAPHDQEEGDVGLKLY
LSKEDLKKLHDFEEQCVEKYFHEKMEDVNCSCEERIRVTSERVTEMYFQLKEMNEKVS
FIKDSLLSLDSQVGHLQDLSALTVDTLKVLSAVDTLQEDEALLAKRKHSTCKKLPHSWS
NVICAEVLGSMEIAGEKKYQYYSMPSSLLRSLAGGRHPPRVQRGALLEITNSKREATNV
RNDQERQETQSSIVVSGVSPNRQAHSKYGQFLLVPSNLKRVPFSAETVLPLSRPSVPDVL
ATEQDIQTEVLVHLTGQTPVVSDWASVDEPKEKHEPIAHLLDGQDKAEQVLPTLSCTPE
PMTMSSPLSQAKIMQTGGGYVNWAFSEGDETGVFSIKKKWQTCLPSTCDSDSSRSEQHQ
KQAQDSSLSDNSTRSAQSSECSEVGPWLQPNTSFWINPLRRYRPFARSHSFRFHKEEKLM
KICKIKNLSGSSEIGQGAWVKAKMLTKDRRLSKKKKNTQGLQVPIITVNACSQSDQLNP
EPGENSISEEEYSKNWFTVSKFSHTGVEPYIHQKMKTKEIGQCAIQISDYLKQSQEDLSKN
SLWNSRSTNLNRNSLLKSSIGVDKISASLKSPQEPHHHYSAIERNNLMRLSQTIPFTPVQL
FAGEEITVYRLEESSPLNLDKSMSSWSQRGRAAMIQVLSREEMDGGLRKAMRVVSTWS
EDDILKPGQVFIVKSFLPEVVRTWHKIFQESTVLHLCLREIQQQRAAQKLIYTFNQVKPQ
TIPYTPRFLEVFLIYCHSANQWLTIEKYMTGEFRKYNNNNGDEITPTNTLEELMLAFSHW
TYEYTRGELLVLDLQGVGENLTDPSVIKPEVKQSRGMVFGPANLGEDAIRNFIAKHHCN
SCCRKLKLPDLKRNDYSPERINSTFGLEIKIESAEEPPARETGRNSPEDDMQL

Figure 9B

GTATCAGGACTCAGCCCATTTCCCCCTCTGGTGCTGAGAAATGGAGGCCGAAGGAGTGATCTAGAAGTGTTAATTGAGCCCCTAATCTATGCTAGTTACTGGGGG
TGTTGGGGGAGACAGGAGAGAGATCCCACGGGGTTCCGGCCTCCCAGGGACTCAGGTCACTAATGGAGGTGGCTTGGCTTGTCTATGTGCTGGGCCAACAGCCA
CTGGCGAGGCAAGGCGAGGGTCAGTCACGGCTGGTGCCAGGAAGAGGGCTGGTTCTTTGGCTCCCTGGTCTCCCGCGGTCTAGCCCAAGCTGGCCAGCGGTTGAC
CTGGCTCCCCTGGCCCCGGCCAGGCCTCGTGGACCCCTCATATGCCACACGGGACATGAGCAGGCCGGCCGGGAGCCGGGTCCCGGGAGCTCCACGAAGGGGCC
TGTCCTCCATGACCAGGACACCCGCTGCGCCTTCCTCCCGAGGCCTCCCGGGCCTCTCCAGACGCGGCGCTACTGCAGACACCAGGGCCGCCAAGGGAGCGGACT
CGGAGCCGGCCCTGGGGCGGGCACATGGGCCCCGGCGCCCCCGGCGTCTCCAAGCCGCGCTGCCCGGGTCGGGCCAGGCCAGGGGAGGGACAGCAGCAGGTG
ACGACGGCCCGGCCACCGGCTATAAATAGGGGCGCGCGTCAGCCGCGGGCGGGAGCGGCGGCGGCGGGCAGGGGCCCGGGGGCCGGGGCCTGGAGGACAGGC
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GTCTCACCCCAGCTCTGGAAGGAGCACCTTCTGCTCCATCATTGCTCAGCTCACAGAGGAGACCCAGCCGCTATTTGAGACCACGCTCAAGTCCCGGTCTGTGTCC
GAGGACAGCGACGTCAGGTTCACCTGCATCGTCACAGGATACCCAGAGCCAGAGGTGACCTGGTACAAGGATGATACGGAGCTGGACCGCTACTGTGGCTTGCC
AAAATATGAGATCACTCATCAGGGCAACCGCCACACACTGCAGCTGTACAGGTGTCGAGAAGAAGATGCCGCCATCTACCAGGCCTCTGCCCAGAACAGCAAGG
GCATTGTGTCCTGCTCAGGGGTCCTGGAGGTGGGCACCATGACTGAGTACAAGATCCACCAGCGCTGGTTCGCCAAGTTGAAGCGCAAGGCTGCGGCAAAGCTG
CGCGAGATCGAGCAGAGCTGGAAGCACGAGAAGGCGGTGCCTGGGGAGGTCGACACTCTGCGCAAGCTCAGCCCCGACCGCTTCCAGCGAAAGCGGCGATTGA
GCGGGGCTCAAGCGCCGGGCCCCTCGGTCCCTACCAGGGAGCCTGAGGGTGGGACCCTGGCGGCTTGGCAGGAGGGAGAGACTGAGACTGCTCAGCACTCAGGT
TTGGGCCTGATCAACAGTTTTGCTTCTGGAGAAGTGACCACCAACGGGGAGGCTGCCCCCGAGAATGGAGAGGACGGAGAGCATGGCTTGCTGACATACATCTG
TGACGCCATGGAGCTGGGGCCTCAGAGAGCCCTCAAAGAGGAGAGTGGGGCCAAGAAGAAAAAGAAAGATGAGGAATCCAAGCAAGGCCTGCGGAAGCCAGA
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GACCCTGAGTGTCCGGGCGCCTGGGGAGAGTCCCAAGGGGAAGGCACCCCTCAGGGCTAGAAGCGAGGGGGTGCCTGGCGCTCCTGGCCAGCCCACACACTCCT
TGACCCCCCAGCCGACTAGGCCTTTCAACAGAAAGAGATTTGCCCCTCCAAAGCCCAAAGGAGAGGCCACCACTGACAGCAAGCCCATTTCTTCTCTGAGTCAAG
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CGGGTCCTAGAGCTCCTCTGAATATTGAATGTTTTGTACAGACCCCAGAAGGGTCTTGTTTCCCAAAAAAACCTGGTTGCCTGCCCAGATCTGAGGAGGCAGTAG
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GTAGCACCCCGACTTCTCAGCACGGGAGCACAGCCACCTTCCTGCCCTCTGAGGATCAGGTCCTGATGAGTTCTGCCCCAACACTGCACCTGGGGCTGGGGACCC
CCACTCAGAGTCACCCACCAGAAACCATGGCCACCAGCAGTGAGGGGGCCTGCGCCCAGGTACCAGATGTGGAGGGGCGGACCCCAGGTCCCCGGAGCTGTGAC
CCTGGCCTCATAGATTCCCTGAAGAACTACCTGCTTCTGCTGCTGAAGCTGTCCAGCACAGAGACAAGTGGAGCAGGGGGAGAGTCCCAGGTGGGGGCAGCCAC
CGGAGGTCTGGTGCCCTCAGCCACTCTGACACCCACTGTGGAAGTGGCTGGGCTTAGTCCCCGGACATCGAGGCGCATCCTGGAGCGTGTGGAGAACAACCACCT
GGTGCAGAGTGCACAGACCCTGCTGCTGAGCCCCTGTACCTCCCGCCGCCTCACCGGCCTCCTGGACCGTGAGGTGCAGGCTGGCCGCCAGGCCCTTGCTGCTGC
CCGAGGCTCCTGGGGTCCTGGTCCCAGCTCCCTCACTGTCCCTGCCATTGTGGTAGACGAGGAGGACCCTGGGCTGGCCTCAGAAGGAGCCAGTGAGGGTGAAG
GAGAGGTTTCCCTTGAGGGGCCTGGCCTCCTGGGGGCCTCTCAGGAGAGCAGCATGGCTGGTCGACTGGGGGAGGCGGGTGGGCAGGCAGCCCCTGGACAGGGG
CCCTCAGCAGAGAGCATAGCCCAGGAGCCCTCCCAAGAGGAGAAGTTCCCAGGGGAGGCTCTGACAGGCCTCCCGGCAGCTACACCTGAGGAACTGGCTCTAGG

Figure 10A

GGCCCGGAGGAAGAGATTTCTCCCTAAGGTCAGAGCAGCAGGAGACGGGGAGGCAACCACACCTGAAGAAAGGGAGAGCCCCACGGTTTCCCCCCGGGGGCCC
AGGAAAAGCCTGGTGCCTGGGTCCCCAGGGACTCCAGGGCGGGAGAGACGCTCCCCTACGCAGGGCAGAAAGGCGAGCATGCTGGAGGTGCCTCGGGCAGAGG
AGGAGCTGGCGGCAGGAGACCTGGGCCCCAGCCCCAAGGCCGGCGGTCTGGACACAGAGGTGGCCCTGGATGAAGGCAAGCAGGAGACACTGGCCAAGCCCAG
GAAAGCCAAAGACCTGCTGAAAGCCCCACAGGTGATCCGGAAGATTCGGGTGGAGCAGTTTCCTGATGCCTCCGGTAGCCTGAAGCTGTGGTGCCAGTTTTTCAA
CATTCTTAGTGACTCAGTCTTGACATGGGCCAAGGATCAGCGCCCAGTGGGCGAGGTGGGCAGGAGCGCAGGGGATGAGGGGCCGGCGGCCTTGGCCATCGTGC
AGGCCTCCCCCGTAGACTGCGGTGTGTATCGGTGCACCATCCACAATGAGCACGGCTCGGCCTCCACCGACTTCTGCCTCAGCCCTGAGGTGTTGTCAGGATTCAT
CTCCAGAGAAGAAGGTGAAGTTGGAGAAGAGATTGAGATGACCCCTATGGTGTTTGCTAAGGGTCTGGCTGACTCTGGCTGCTGGGGGGACAAGCTCTTTGGGC
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CGCACGTGCATCATCAAGGTGTCCAGCCTGCTTGTGTTTGGGCCCAGCAGTGAGACTTCTCTTGTGGGCAGAAACTACGACGTCACCATCCAGGGGTGCAAGATC
CAGAACATGAGTCGGGAGTACTGCAAAATCTTCGCAGCAGAAGCCCGGGCCGCGCCTGGCTTTGGGGAGGTGCCTGAGATCATCCCACTGTATCTGATCTACCGG
CCTGCAAACAATATCCCATATGCTACCCTGGAGGAAGACCTGGGCAAGCCCCTGGAGTCTTACTGTTCTCGGGAATGGGGCTGTGCTGAGGCTCCGACAGCATCT
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GCCTACTGTGAGCTGCTGGGGCTGACACCTCTCAAGGGCCCGGAGGCGGCCCACCCCCAAGCCAAAGCCAAAGGCTCTAAGAGTCCATCTGCTGGCAGGAAAGG
CTCCCAGCTGAGTCCTCAGCCCCAGAAGAAAGGCCTCCCTAGTCCTCAGGGCACCCGGAAGAGTGCTCCAAGTTCCAAGGCCACCCCTCAGGCCTCAGAGCCAGT
CACCACTCAGTTGTTGGGACAGCCTCCCACCCAAGAGGAGGGCTCCAAGGCCCAGGGCATGCGGTAGCCTCTGCAGAGGCTGGGGGCCTCCACCCAGCAGCAGA
CCAACCAGGAAGCAGCTTGAACTGGATGGAGACTTTCCAAATATGGAACTAACTGGAGAAGGTGCACGAAGGAGACACCACTTGGGGACCTCTCTGAGCAGGCT
CTCGTGAATCAGCTCGTCATCAGATGGCTTTGGTGCATGGCACATAGCCCACTGGCCTCTTCTGGTGCCACTGTCACCCAGGGCTCCCGGGCCTCAAGCAGTCCCC
ACCTCCGAGTGCCTGGCAACCTAGGCCCTCCTTGAAGTTTACACTTTGCCACTGCTGGAGGCTCCCCTGAGTCCTCTGCATGAGTTCTGCACCCCAAGCCCTTGCC
CCAGCCCAGTCCAGCAGCAGATGTTACAATCTGAGTGAGGACATGCAGGCCAACTTTTACCCTCCTGCATTTGCCTGGCCCTGATCTCGCCTGTCCTCAGGGATCC
AGACTTCCTCTGCTGGTCTGGCCTGGTGACTCTCAGGGTATCTTCTCCTTCCAGCTACTTTCGCTCACTGATCTCAGCTTATCCTGCAACTAACCATCCTTGAGCCC
AGATGGGGCTCAGGGCCCTTCCAGAGCCTGTCATGTCCTTGTGCAGTGGCCTTTGATGTGTGTTCACGCTCTTCCCCCTTCACTCACTCGCCTGCTTCCCATGCTCC
CTTGTACCCCCTCGCCACATCCCTGTCTTGGGGCCCAGCTGCAGCCTGCTGCCTGCCCTTCATGGCTCTGCACATGGCCCTTTGCTTGAGGGCTCCCCACTCCCTGC
CCACCAATACCCAGGTGAGGAACAGACCCTCTGGCCTCTCACCCCACTTCAGTGCTCTCTTCCCCAACTTCTCTCGGGCTCTTTGCTCATGAGGTGAGAGCTGGTG
TGAGGGTTGTGTCAGCAGCTGTAGCCAGAGAGAGGTGTTGACTCTGAGAGACCTTGCACTCCATACTGAAAGGAGGTGGGGTCACAGTGAATTTCACATCCCCTC
TCAACCAGGAGTGGAGGGCTAGGTCCCTTCCCCATGGGGAGTACACTTGGGTGTTCTAGGAGGGATGCAGTCTATCCATGCACTTGGGTGGAGGGGAGTCTCTGT
GCCTGGGAATTAGGACCCCTGCTCCAACCATCGCTCTTGATCCTGGGGCCCCAGCTCTGGGTCCTCATGTATGGGCTCCCAAGGACCCAGCAGCCTGGATCCTTCC
AGAGCATCCCTCCTGGAGGCCTGGGATGGGGTAGGTCTGCAGCTAGCCTACTCCCTTTGGAATGCAATAAAGGCAGCATTGTGTGCCCTGCTTGCCCTCATCTGGT
GTGGTTGGAGGTCTGTGGAGTCAAGGTCCCCCTCTCCCAGGCAGGCTCTCTGAGGGCATTCTGTAGTCCCAGGCCCACTGGAAAAATGAATCTATATTTGGTTCC
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TTACGCCTTTGGAATTGCTCTTCATTCAGAAGAGGAACACAAAGGAAGCCACCCAGGAAGGAAGCACAGAGCTGGGGGCTCTGGAAACGCCCTGTGTCTCTGGC
TACAGCAAGACCAGCCCAGGAGCCCACCAGCACCTGCCTCTCAGCTACTTGCTGACCATTTCCTGCTTCTCAAGCTGCAGAGAAGCTTTTCATTCCCACCCCCACC
CGGAACCTCCCCTTGCCTAACATTTCCCCTCTATGGTAACATCTCTGACTTCTCTACCTCCTCTGTGCTCAGGTGACTCCACATCTTCTGCCCCAGTGTGTCCCCAC
CTCTCCCAGCCTGTATACCCAGATTACTTTGGTGAACTGAAAAA

Figure 10A

601-1-098C17

MEVAWLVYVLGQQPLARQGEGQSRLVPGRGLVLWLPGLPRSSPSWPAVDLAPLAPARPRGPLICHTGHEQAGREPGPGSST
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DRRMQGEKGMQGEKGTQSEGSAPTAMEGQSEQEVATSLGPPSRTPKLPPTAGPRAPLNIECFVQTPEGSCFPKKPGCLPRSEE
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VEGRTPGPRSCDPGLIDSLKNYLLLLLKLSSTETSGAGGESQVGAATGGLVPSATLTPTVEVAGLSPRTSRRILERVENNHLV
QSAQTLLLSPCTSRRLTGLLDREVQAGRQALAAARGSWGPGPSSLTVPAIVVDEEDPGLASEGASEGEGEVSLEGPGLLGAS
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PTVSPRGPRKSLVPGSPGTPGRERRSPTQGRKASMLEVPRAEEELAAGDLGPSPKAGGLDTEVALDEGKQETLAKPRKAKDL
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DLGKPLESYCSREWGCAEAPTASGSSEAMQKCQTFQHWLYQWTNGSFLVTDLAGVDWKMTDVQIATKLRGYQGLKESCF
PALLDRFASSHQCNAYCELLGLTPLKGPEAAHPQAKAKGSKSPSAGRKGSQLSPQPQKKGLPSPQGTRKSAPSSKATPQASEP
VTTQLLGQPPTQEEGSKAQGMR

Figure 10B

ATGAATAATCAAAAAGTGGTAGCTGTGCTACTGCAAGAGTGCAAGCAAGTGCTGGATCAGCTCTTGTTGGAAGCGCCAGATGTGTCGGAAGAGGACAAGAGCGA
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GTCGCAGAGCAGGGCATCGACCCTGATGCCTCCACAGTGGATGAGGAGGGGCAACTGCTCGACAGCATGGATGTTCCCTGCACAAATGGGCACGGCTCTCATAG
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TTTAGAGGACAAGACAATAAAGGGATGTATCAGTGTGGAGCCTTACATACTGGGAGAATTTGTAAAATTGTCAAATAACACGAAAGTGGTGAAAACAGAATACA
AAGCCACAGAATATGGCTTGGCCTATGGCCATTTTTCTTATGAGTTTTCTAATCATAGAGATGTTGTGGTCGATTTACAAGGTTGGGTAACCGGTAATGGAAAAGG
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GAATGTAATGAAATCTGCCATCGTCTTTCTTTGACTAGACCTTCAATGGAGAAACCA

Figure 11A

MNNQKVVAVLLQECKQVLDQLLLEAPDVSEEDKSEDQRCRALLPSELRTLIQEAKEMKWPFVPEKWQY
KQAVGPEDKTNLKDVIGAGLQQLLASLRASILARDCAAAAAIVFLVDRFLYGLDVSGKLLQVAKGLHKL
QPATPIAPQVVIRQARISVNSGKLLKAEYILSSLISNNGATGTWLYRNESDKVLVQSVCIQIRGQILQKLGM
WYEAAELIWASIVGYLALPQPDKKGLSTSLGILADIFVSMSKNDYEKFKNNPQINLSLLKEFDHHLLSAA
ACKLAAAFSAYTPLFVLTAVNIRGTCLLSYSSSNDCPPELKNLHLCEAKEAFEIGLLTKRDDEPVTGKQEL
HSFVKAAFGLTTVHRRLHGETGTVHAASQLCKEAMGKLYNFSTSSRSQDREALSQEVMSVIAQVKEHLQ
VQSFSNVDDRSYVPESFECRLDKLILHGQGDFQKILDTYSQHHTSVCEVFESDCGNNKNEQKDAKTGVCI
TALKTEIKNIDTVSTTQEKPHCQRDTGISSSLMGKNVQRELRRGGRRNWTHSDAFRVSLDQDVETETEPSD
YSNGEGAVFNKSLSGSQTSSAWSNLSGFSSSASWEEVNYHVDDRSARKEPGKEHLVDTQCSTALSEELEN
DREGRAMHSLHSQLHDLSLQEPNNDNLEPSQNQPQQQMPLTPFSPHNTPGIFLAPGAGLLEGAPEGIQEVR
NMGPRNTSAHSRPSYRSASWSSDSGRPKNMGTHPSVQKEEAFEIIVEFPETNCDVKDRQGKEQGEEISERG
AGPTFKASPSWVDPEGETAESTEDAPLDFHRVLHNSLGNISMLPCSSFTPNWPVQNPDSRKSGGPVAEQGI
DPDASTVDEEGQLLDSMDVPCTNGHGSHRLCILRQPPGQRAETPNSSVSGNILFPVLSEDCTTTEEGNQPG
NMLNCSQNSSSSSVWWLKSPAFSSGSSEGDSPWSYLNSSGSSWVSLPGKMRKEILEARTLQPDDFEKLLA
GVRHDWLFQRLENTGVFKPSQLHRAHSALLLKYSKKSELWTAQETIVYLGDYLTVKKKGRQRNAFWVH
HLHQEEILGRYVGKDYKEQKGLWHHFTDVERQMTAQHYVTEFNKRLYEQNIPTQIFYIPSTILLILEDKTIK
GCISVEPYILGEFVKLSNNTKVVKTEYKATEYGLAYGHFSYEFSNHRDVVVDLQGWVTGNGKGLIYLTD
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Figure 11B

FIGURE 12

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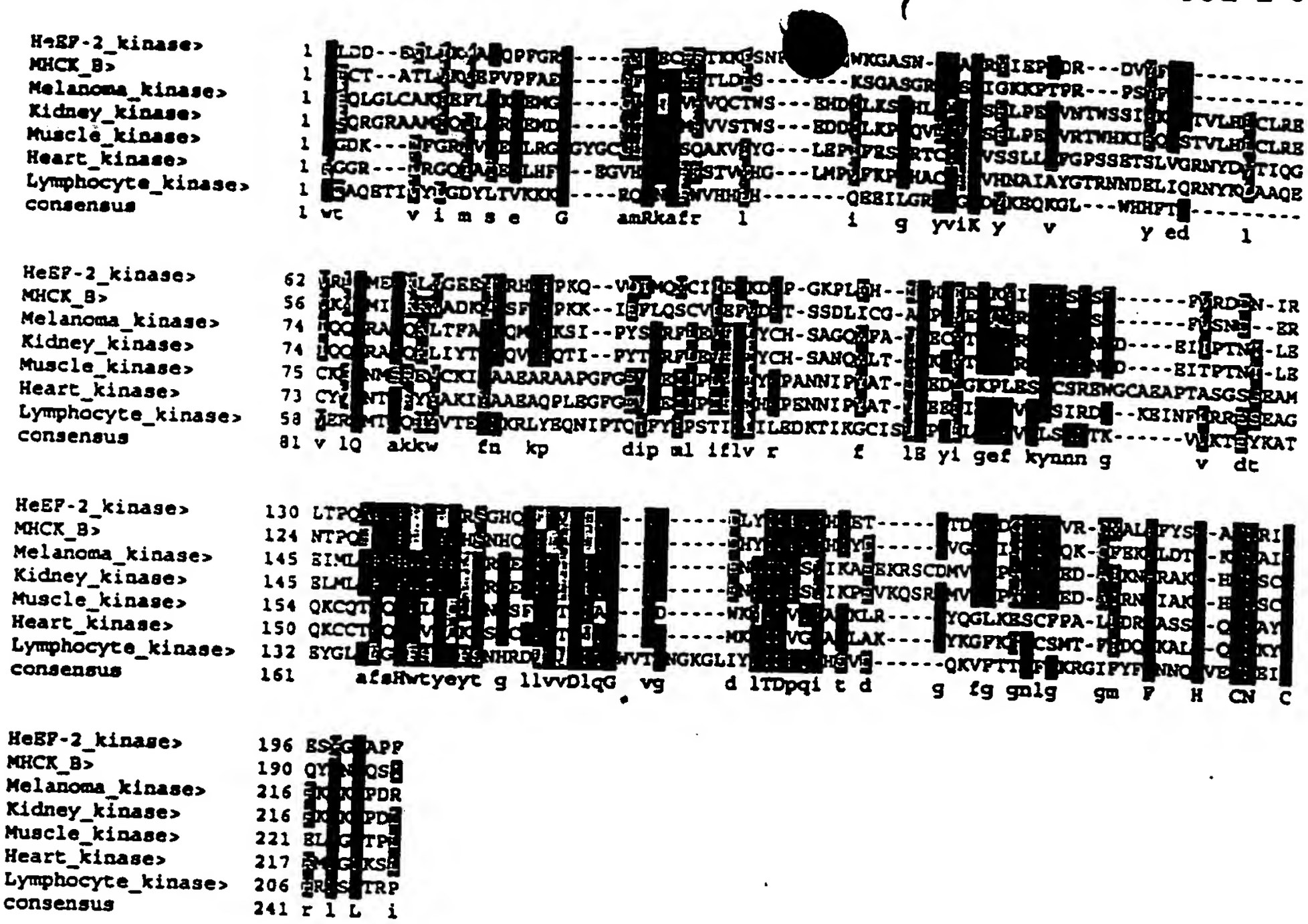

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PHYLOGENETIC TREE OF ALPHA-KINASES

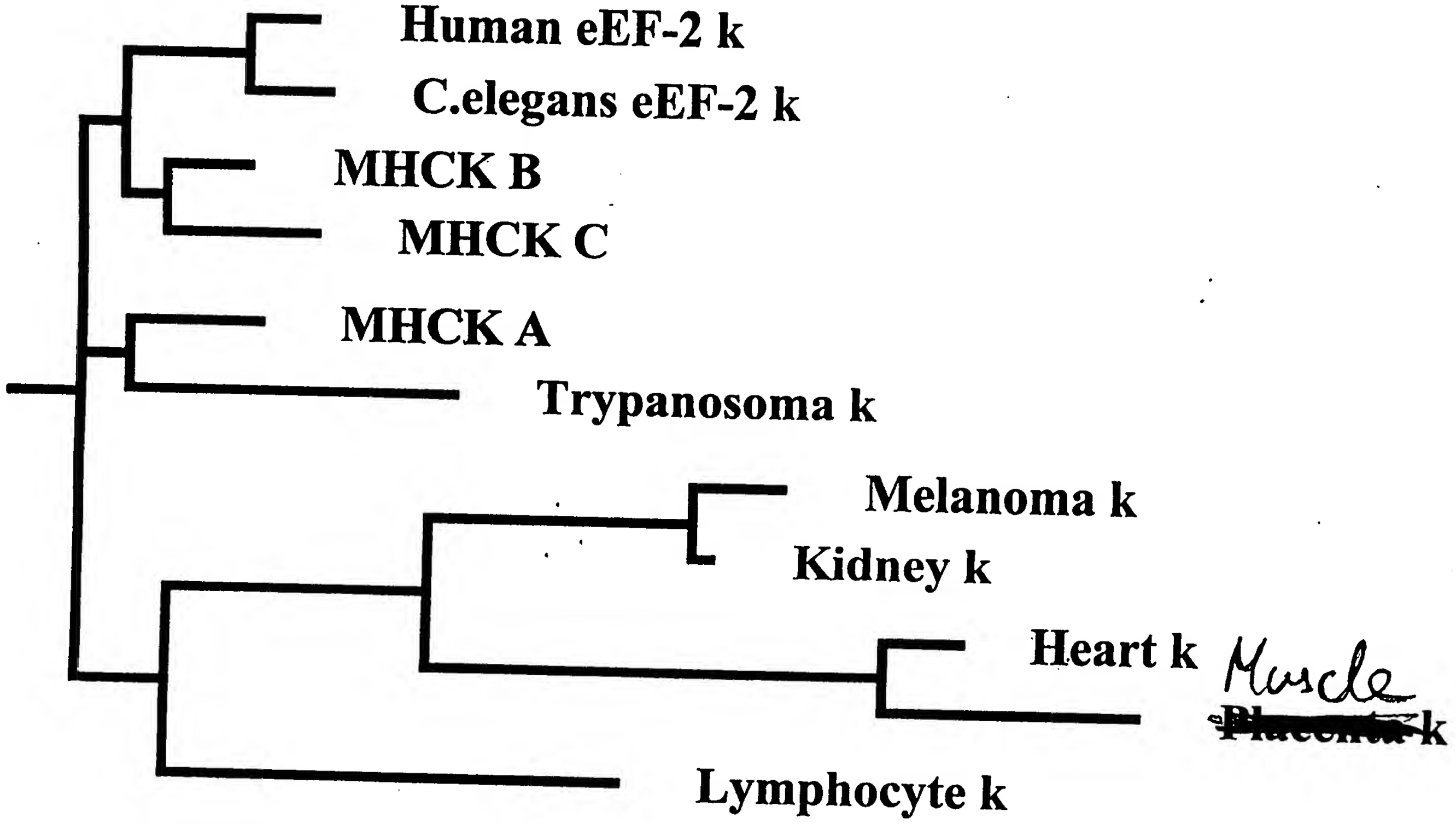


FIGURE 13

FIGURE 14 Sheet 25 of 31 **601-1-098C1**

Time curve

melanoma kinase
catalytic domain.

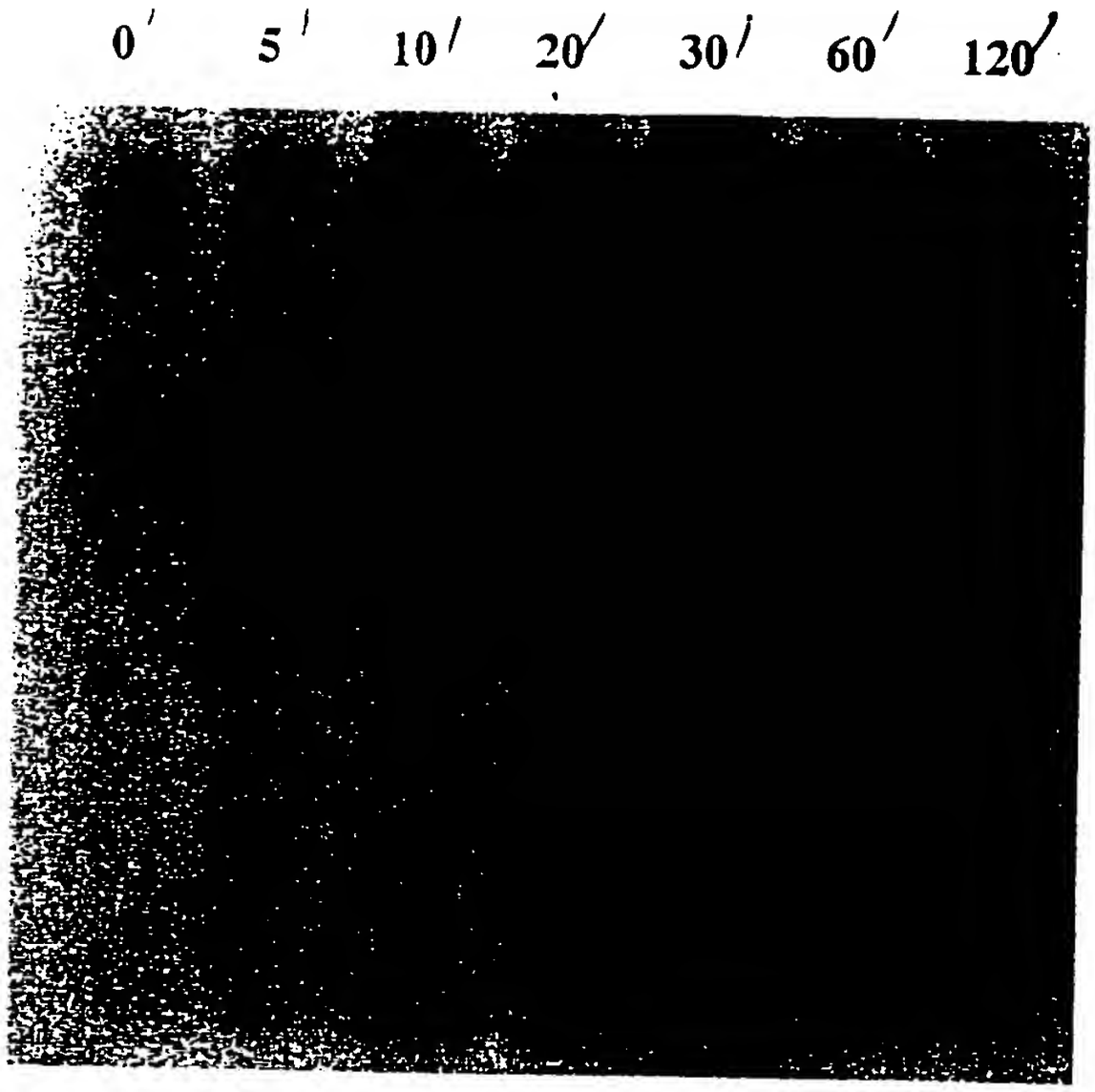
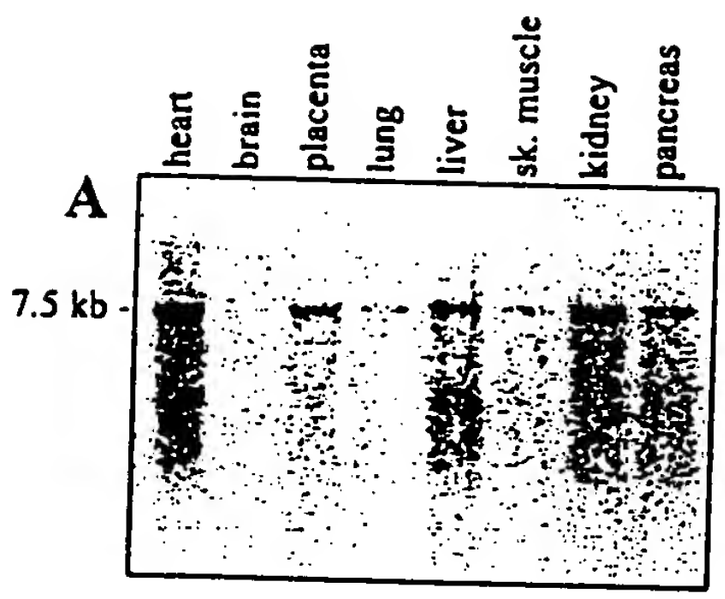
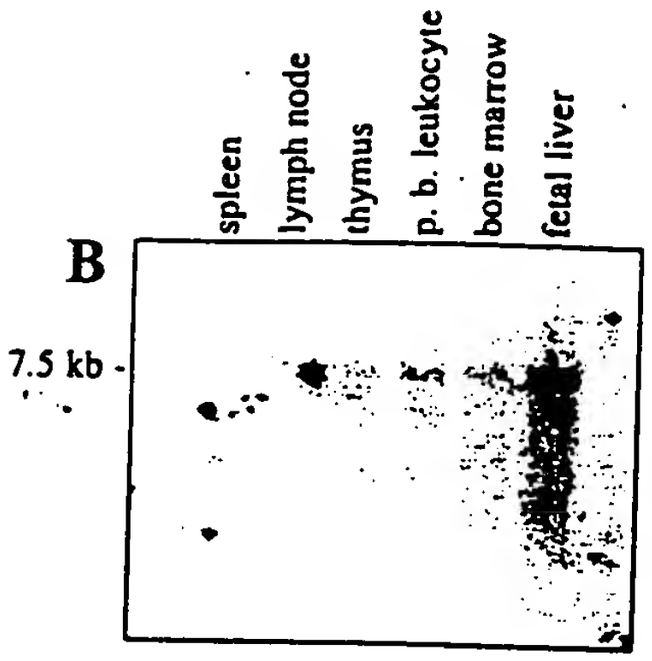
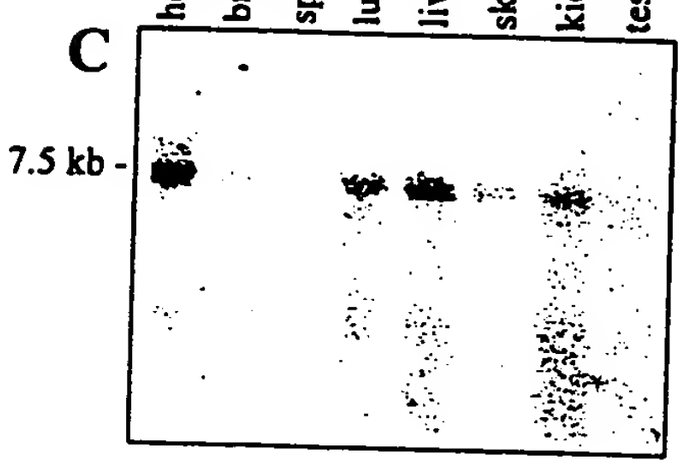
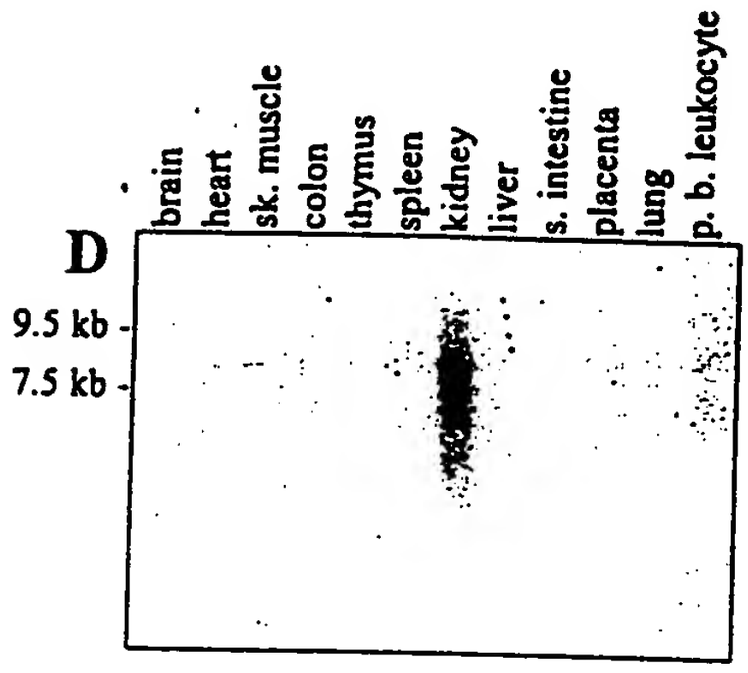


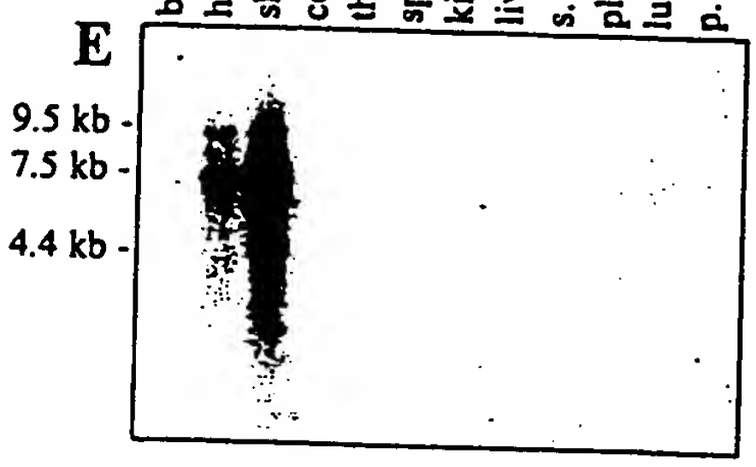
FIGURE 15


A
heart
brain
placenta
lung
liver
sk. muscle
kidney
pancreas
7.5 kb -


B
spleen
lymph node
thymus
p. b. leukocyte
bone marrow
fetal liver
7.5 kb -


C
heart
brain
spleen
lung
liver
sk. muscle
kidney
testes
7.5 kb -


D
brain
heart
sk. muscle
colon
thymus
spleen
kidney
liver
s. intestine
placenta
lung
p. b. leukocyte
9.5 kb -
7.5 kb -


E
brain
heart
sk. muscle
colon
thymus
spleen
kidney
liver
s. intestine
placenta
lung
p. b. leukocyte
9.5 kb -
7.5 kb -
4.4 kb -

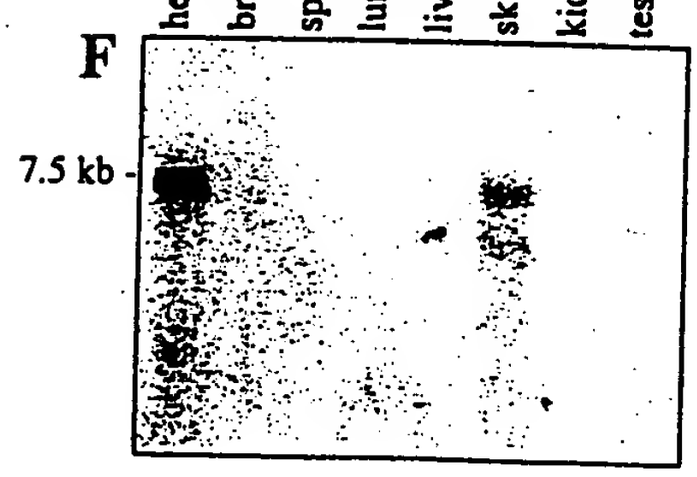

F
heart
brain
spleen
lung
liver
sk. muscle
kidney
testes
7.5 kb -

FIGURE 16

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601-1-098 CIP

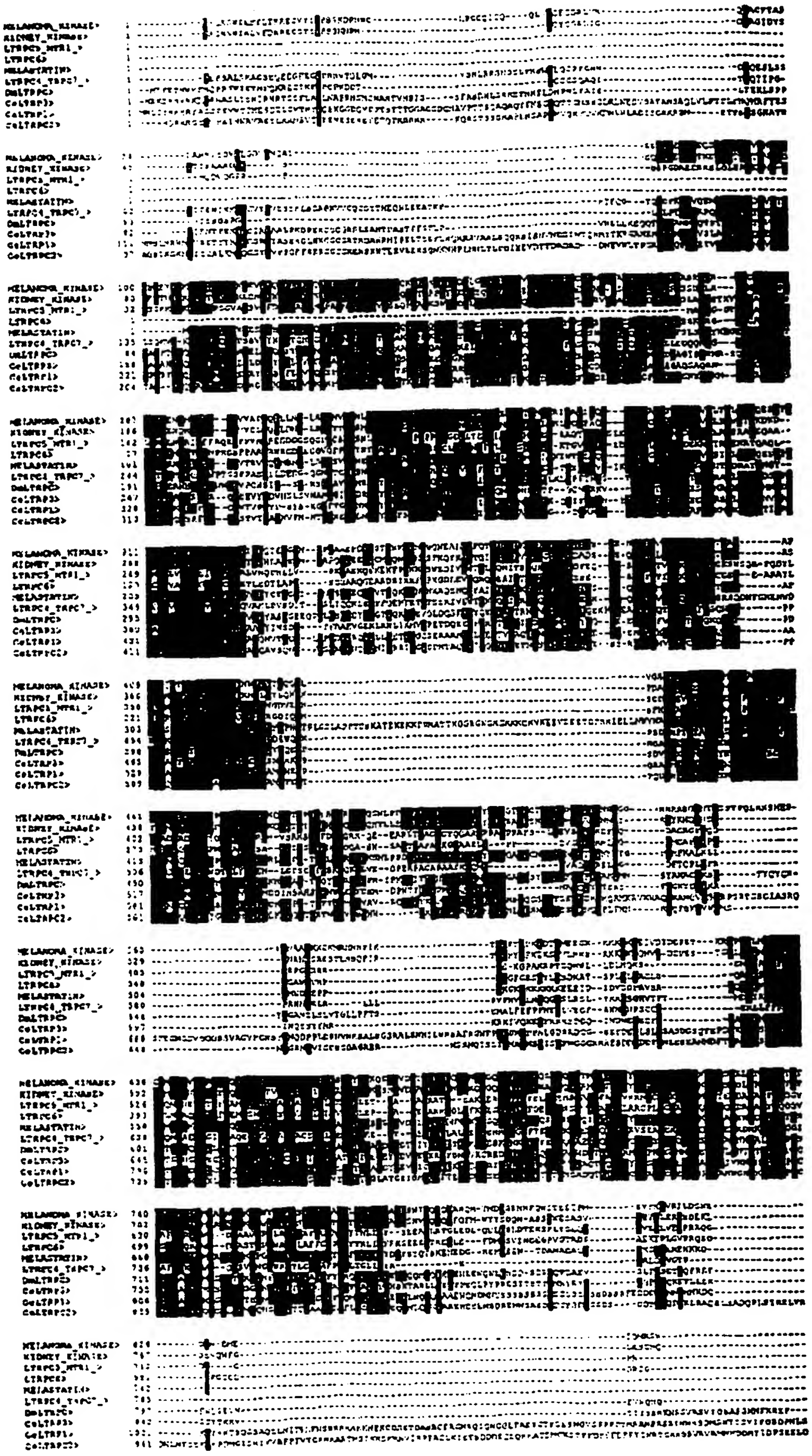


Figure 17

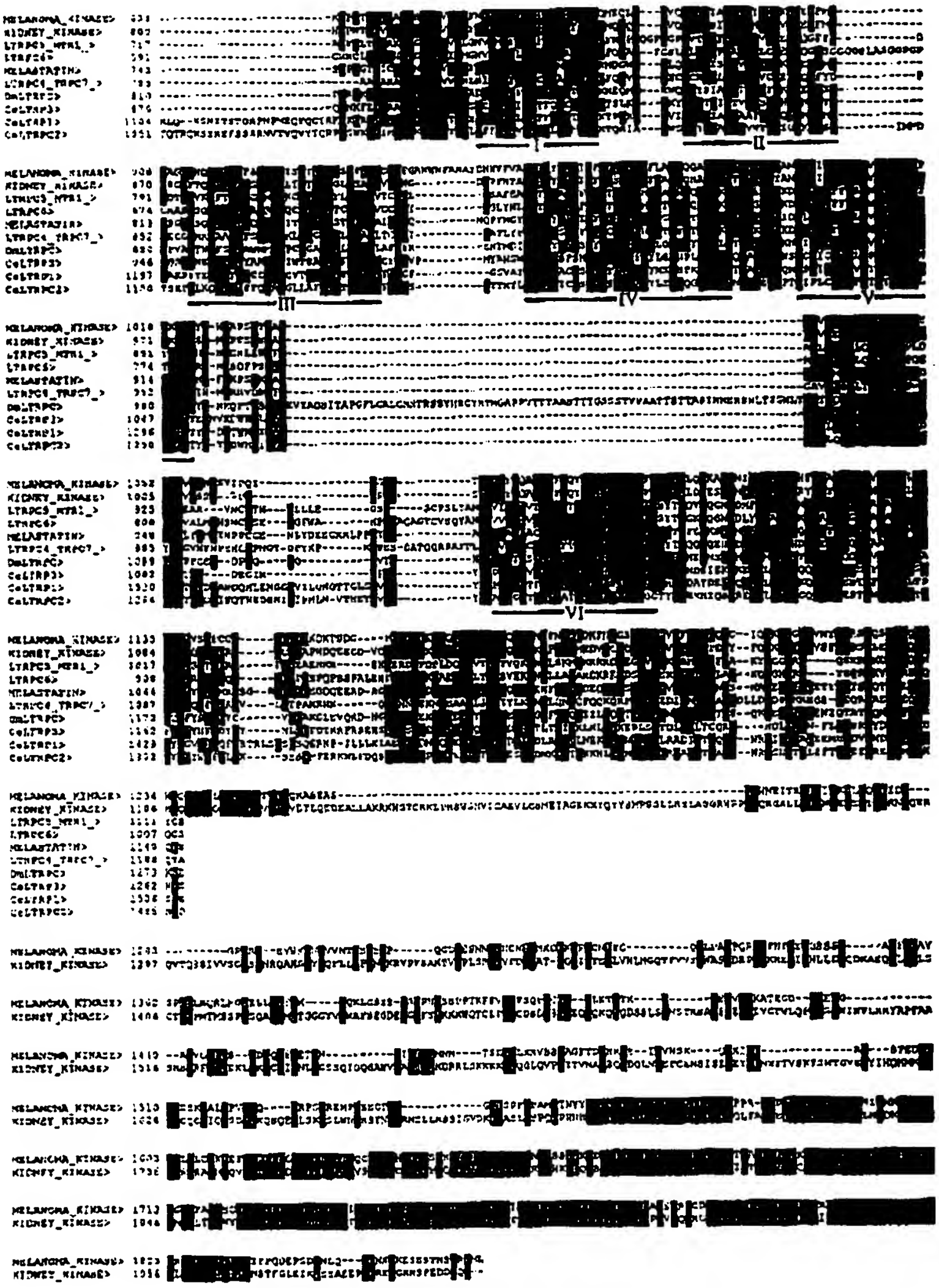


Figure 17

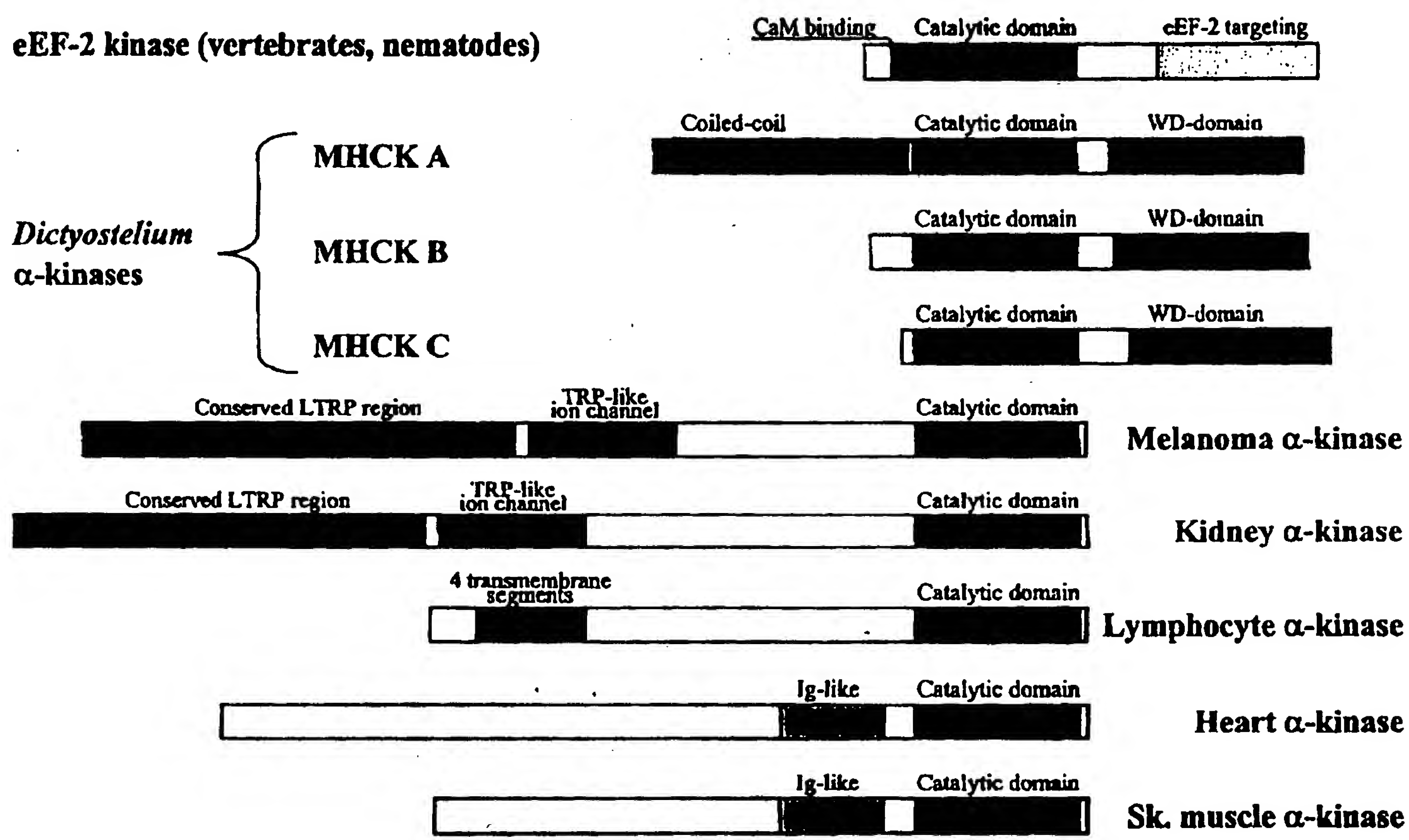
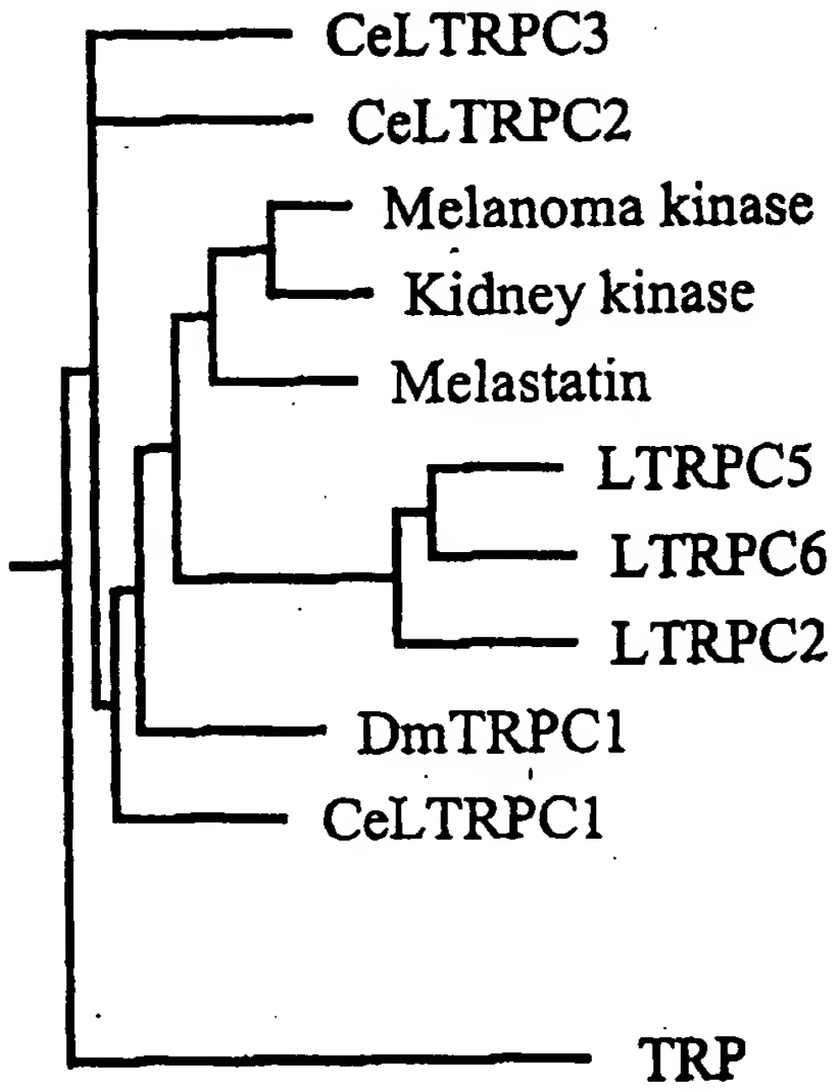


Figure 18

A



B

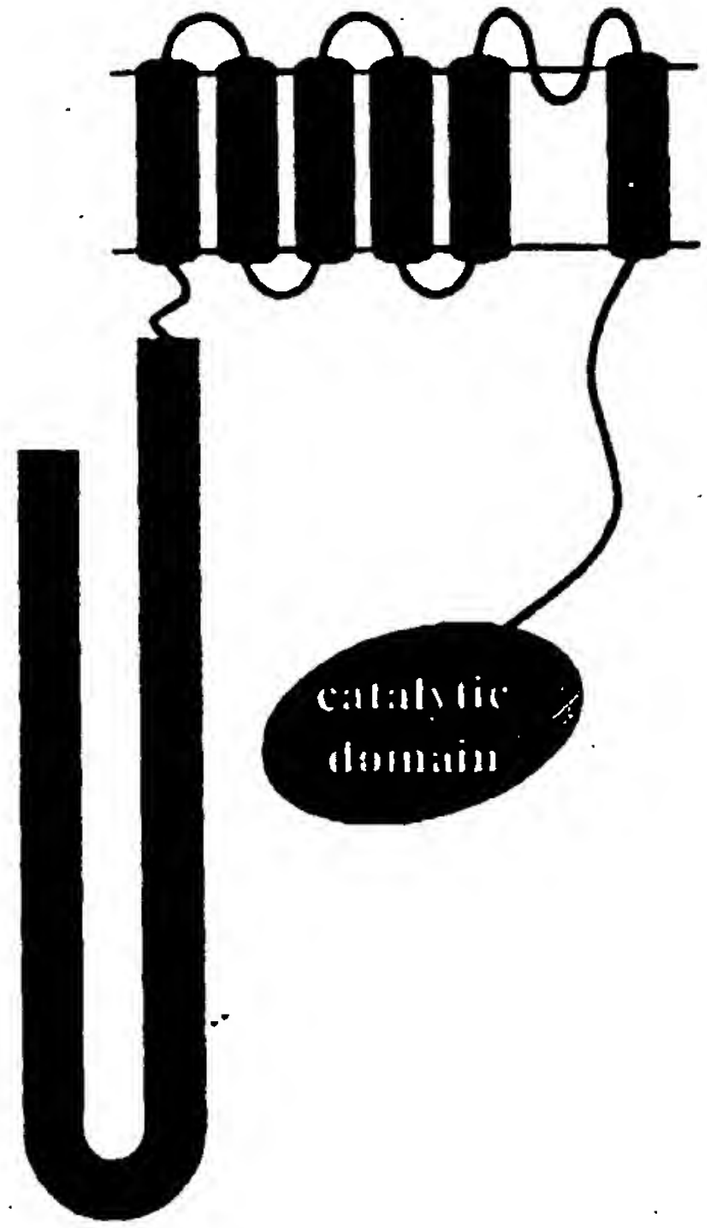


Figure 19A&B